Claims

1. (original) A method for the controlled-release of an active substance into a use environment, comprising:

a. preparing a controlled-release delivery composition comprising an active-substance-containing core and an asymmetric polymeric coating thereon, wherein the polymer used to form said asymmetric polymeric coating is one which, when tested by soaking for at least 16 hours in an aqueous solution comprising 0.5 wt% dietary fat, gains less than about 15 wt%; and

b. administering said composition to said use environment, said use environment comprising at least about 0.5 wt% of dietary fat.

2. (original) A method for the controlled-release of an active substance into a use environment, comprising:

a. preparing a controlled-release delivery composition comprising an active-substance-containing core and an asymmetric polymeric coating thereon, wherein the time to release 50% of said active substance from said composition into said use environment is at least 0.5-fold, but less than 2.0-fold the time required for said composition to release 50% of said active substance into a control use environment comprising less than about 0.1% of dietary fat, and

b. administering said composition to said use environment, said use environment comprising at least about 0.5 wt% of dietary fat.

3. (original) A method for the controlled-release of an active substance into a use environment, comprising:

a. preparing a controlled-release delivery composition comprising an active-substance-containing core and an asymmetric polymeric coating thereon, wherein the amount of drug released from said composition at any time between the 2nd and 10th hour following introduction of said composition to said use environment is at least 0.5-fold, but less than 2.0-fold the amount of

said drug released at the same time between the 2nd and 10th hour by said composition into a control use environment comprising less than about 0.1% of dietary fat, and

b. administering said composition to said use environment,
said use environment comprising at least about 0.5 wt% of dietary fat.

4. (original) A method for the controlled-release of an active substance into a use environment, comprising:

a. preparing a controlled-release delivery composition comprising an active-substance-containing core and an asymmetric polymeric coating thereon, wherein the average rate of drug release from said composition between the 2nd and 10th hour after introduction into said use environment is at least 0.5-fold, but less than 2.0-fold the average rate of drug release provided by said composition in a control use environment comprising less than about 0.1% of dietary fat, and

b. administering said composition to said use environment,
said use environment comprising at least about 0.5 wt% of dietary fat.

5. (original) A method for the controlled-release of an active substance into a use environment, comprising:

a. preparing a controlled-release delivery composition comprising an active-substance-containing core and an asymmetric polymeric coating thereon, wherein the composition provides a maximum concentration of said active substance in said use environment that is at least 0.5-fold, but less than 2.0-fold the maximum concentration provided by said composition in a control use environment comprising less than about 0.1% of dietary fat, and

b. administering said composition to said use environment,
said use environment comprising at least about 0.5 wt% of dietary fat.

6. (original) A method for the controlled-release of an active substance into a use environment, comprising:

a. preparing a controlled-release delivery composition comprising an active-substance-containing core and an asymmetric polymeric coating thereon, wherein the composition provides an area under the active substance concentration versus time curve (AUC) for any period of at least 90 minutes between the time of introduction to said use environment and about 270 minutes following introduction to said use environment that is at least 0.5-fold, but less than 2.0-fold the AUC provided by said composition in a control use environment comprising less than about 0.1% of dietary fat, and

b. administering said composition to said use environment, said use environment comprising at least about 0.5 wt% of dietary fat.

7. (original) A method for the controlled-release of an active substance into a use environment, comprising:

a. preparing a controlled-release delivery composition comprising an active-substance-containing core and an asymmetric polymeric coating thereon, wherein the composition provides a relative bioavailability in said use environment that is at least 0.5-fold, but less than 2.0-fold the relative bioavailability provided by said composition in a control use environment comprising less than about 0.1% of dietary fat, and

b. administering said composition to said use environment, said use environment comprising at least about 0.5 wt% of dietary fat.

8. (currently amended) A therapeutic package, comprising:

a container,

a controlled-release delivery composition for the controlled release of an active substance into a use environment, comprising an active-substance-containing core and an asymmetric polymeric coating thereon, wherein said delivery composition satisfies any one or more of the following conditions (i) through (vii):

(i) the polymer used to form said polymeric coating is one which, when tested by soaking for at least 16 hours in an aqueous solution comprising 0.5 wt% dietary fat, gains less than about 15 wt%;

(ii) the time to release 50% of said active substance from said composition into said use environment is at least 0.5-fold, but less than 2.0-fold the time required for said composition to release 50% of said active substance into a control use environment comprising less than about 0.1% of dietary fat;

(iii) the amount of drug released from said composition at any time between the 2nd and 10th hour following introduction of said composition to said use environment is at least 0.5-fold, but less than 2.0-fold the amount of said drug released at the same time between the 2nd and 10th hour by said composition into a control use environment comprising less than about 0.1% of dietary fat;

(iv) the average rate of drug release from said composition between the 2nd and 10th hour after introduction into said use environment is at least 0.5-fold, but less than 2.0-fold the average rate of drug release provided by said composition in a control use environment comprising less than about 0.1% of dietary fat;

(v) the composition provides a maximum concentration of said active substance in said use environment that is at least 0.5-fold, but less than 2.0-fold the maximum concentration provided by said composition in a control use environment comprising less than about 0.1% of dietary fat;

(vi) the composition provides an area under the active substance concentration versus time curve (AUC) for any period of at least 90 minutes between the time of introduction to said use environment and about 270 minutes following introduction to said use environment that is at least 0.5-fold, but less than 2.0-fold the AUC provided by said composition in a control use environment comprising less than about 0.1% of dietary fat; ~~or~~and

(vii) the composition provides a relative bioavailability in said use environment that is at least 0.5-fold, but less than 2.0-fold the relative bioavailability

provided by said composition in a control use environment comprising less than about 0.1% of dietary fat,

and, associated with said package, written matter non-limited as to whether the dosage form can be taken with or without food.

9. (original) A method as claimed in any one of claims 1-7, or a therapeutic package as claimed in claim 8, wherein said controlled-release delivery composition is embodied as an osmotic dosage form.

10. (original) A method or therapeutic package as claimed in claim 9, wherein said osmotic dosage form comprises a homogeneous core, a bursting osmotic core, or a bursting coated swelling core.

11. (original) A method as claimed in any one of claims 1-7, or a therapeutic package as claimed in claim 8, wherein said controlled-release delivery composition is embodied as a hydrogel-driven device.

12. (original) A method as claimed in any one of claims 1-7, or a therapeutic package as claimed in claim 8, wherein said controlled-release delivery composition is embodied as a diffusion device.

13. (original) A method as claimed in any one of claims 1-7, or a therapeutic package as claimed in claim 8, wherein said active substance is selected from antihypertensives, antianxiety agents, anticlotting agents, anticonvulsants, blood glucose-lowering agents, decongestants, antihistamines, antitussives, antineoplastics, beta blockers, antiinflammatories, antipsychotic agents, cognitive enhancers, anti-atherosclerotic agents, cholesterol reducing agents, antiobesity agents, autoimmune disorder agents, anti-impotence agents, antibacterial and antifungal agents, hypnotic agents, anti-Parkinsonism agents, anti-Alzheimer's disease agents, antibiotics, anti-depressants, antiviral agents, glycogen phosphorylase inhibitors, and cholesterol ester transfer protein inhibitors.

14. (original) A method as claimed in any one of claims 1-7, or a therapeutic package as claimed in claim 8, wherein said active substance is selected from prazosin,

nifedipine, amlodipine besylate, trimazosin, doxazosin, glipizide, chlorpropamide, sildenafil, sildenafil citrate, chlorambucil, lomustine, echinomycin, tubulazole, atorvastatin calcium, hydroxyzine hydrochloride, doxepin hydrochloride, betamethasone, prednisolone, aspirin, piroxicam, valdecoxib, carprofen, celecoxib, flurbiprofen, (+)-N-{4-[3-(4-fluorophenoxy)phenoxy]-2-cyclopenten-1-yl}-N-hyroxyurea, phenobarbital, acyclovir, nelfinavir, virazole, retinol, vitamin E, timolol, nadolol, apomorphine, chlorthalidone, spironolactone, dicumarol, digoxin, digitoxin, 17-methyltestosterone, testosterone, desoxycorticosterone, alfaxalone, fluoxymesterone, methanstenolone, sulpiride, [3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-(1-ethylpropyl)-amine, 3,5-dimethyl-4-(3'-pentoxy)-2-(2',4',6'-trimethylphenoxy)pyridine, pyroxidine, fluoxetine, paroxetine, venlafaxine, sertraline, carbenicillin indanylsodium, bacampicillin hydrochloride, troleandomycin, doxycyline hyclate, ampicillin, penicillin G, benzalkonium chloride, chlorhexidine, nitroglycerin, mioflazine, etomidate, acetazolamide, chlorzolamide, econazole, terconazole, fluconazole, voriconazole, griseofulvin, metronidazole, thiabendazole, oxfendazole, morantel, astemizole, levocabastine, cetirizine, loratadine, decarboethoxyloratadine, cinnarizine, ziprasidone, olanzepine, thiothixene hydrochloride, fluspirilene, risperidone, penfluridole, loperamide, cisapride, ketanserin, mianserin, lidocaine, acetohexamide, dimenhydrinate, cotrimoxazole, L-DOPA, THA, donepezil, famotidine, chlordiazepoxide, triazolam, alprostadil, prostacyclin, enalaprilic acid, lisinopril, oxytetracycline, minocycline, erythromycin, clarithromycin, spiramycin, azithromycin, [R-(R*S*)]-5-chloro-N-[2-hydroxy-3-{methoxymethylamino}-3-oxo-1-(phenylmethyl)propyl-1H-indole-2-carboxamide, 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-(2R)-hydroxy-3-((3R,4S)-dihydroxypyrrolidin-1-yl-)-3-oxypropyl]amide, [2R,4S]-4-[3,5-bis-trifluoromethyl-benzyl)-methoxycarbonyl-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester, and [2R,4S]-4-[acetyl-(3,5-bis-trifluoromethyl-benzyl)-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid isopropyl ester.

15. (original) A method as claimed in any one of claims 1-7, or a therapeutic package as claimed in claim 8, wherein said use environment is *in vitro*.

16. (original) A method as claimed in any one of claims 1-7, or a therapeutic package as claimed in claim 8, wherein said use environment is *in vivo*.

17. (original) A method as claimed in any one of claims 1-7, or a therapeutic package as claimed in claim 8, wherein said use environment is the human gastrointestinal tract.

18. (original) A method as claimed in any one of claims 1-7, or a therapeutic package as claimed in claim 8, wherein said use environment contains at least 2.0 wt% of dietary fat.

19. (currently amended) A method as claimed in any one of claims 1-7, or a therapeutic package as claimed in claim 8, further comprising a taste ~~making~~ masking coating surrounding said polymeric coating.

20. (original) A method as claimed in any one of claims 1-7, or a therapeutic package as claimed in claim 8, further comprising an immediate release coating of said active substance surrounding said polymeric coating.

21. (original) A method as claimed in any one of claims 1-7, or a therapeutic package as claimed in claim 8, wherein said asymmetric polymeric coating comprises cellulose acetate, cellulose acetate butyrate, cellulose acetate proprionate, cellulose acetate phthalate, hydroxypropyl methyl cellulose acetate succinate, polymethacrylate, and mixtures and blends thereof.

22. (original) A method as claimed in any one of claims 1-7, or a therapeutic package as claimed in claim 8, wherein said asymmetric polymeric coating comprises cellulose acetate.